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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/525,142	03/14/2000	Pablo Tamayo	2825.1014-001	8330
21005	7590	12/05/2003	EXAMINER	
HAMILTON, BROOK, SMITH & REYNOLDS, P.C. 530 VIRGINIA ROAD P.O. BOX 9133 CONCORD, MA 01742-9133			ZHOU, SHUBO	
		ART UNIT		PAPER NUMBER
		1631		33
DATE MAILED: 12/05/2003				

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/525,142	TAMAYO ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Shubo "Joe" Zhou	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 14 July 2003.
- 2a) This action is FINAL.                  2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-18 is/are rejected.
- 7) Claim(s) 1-18 is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                  | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) Paper No(s). <u>33</u> |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)               |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____  |

**DETAILED ACTION**

Upon further consideration and in view of the telephone interview conducted on 11/19/03, the finality of the Office action mailed 10/1/03 is hereby withdrawn in order to allow applicants to consider the full text reference by Mangiameli et al. to be provided in the present Office action.

***Response to RCE and Amendment***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/14/03 has been entered.

The Examiner acknowledges receipt of the Amendment/Reply accompanying the RCE request filed on 7/14/03, and the amendment has been entered.

Claims 1-18 are currently pending and under consideration.

The rejections of claims 1-18 in the previous Office action under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention (the new matter rejection), have been withdrawn in view of the amendment made to claims 1 and 11 as filed on 7/14/03.

***Claim Objections***

Claims 1-18 are objected to because of the following informalities:

Claims 1 and 11 are amended to contain “wherein prior knowledge of the datapoints to be clustered is not necessary”. The phrase is confusing due to the word “in”. It appears to be a typographical error and should have been “is”.

Claims 2-10, and 12-18 depend from claim 1 or 11 and contain the newly added phrase.

Appropriate correction is required.

***Claim Rejections-35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mack, David H. (US patent no. 6,303,301, date of patent: 10/16/01, filed 5/29/1998), in view of Mangiameli et al. (European J. Operational Research, September 1996, Vol. 93, pages 402-417).**

Mack discloses methods of cluster analysis for gene expression monitoring.

In regard to claim 1, the method by Mack comprises receiving gene expression values of the datapoints, clustering the datapoints, and providing output display indicating the clusters of the datapoints (see Figs 2, 9A and 9B, columns 2, 27-28). Mack cites the method by Harfigan for such cluster analysis. See column 27. However, Mack does not explicitly disclose clustering using self organizing map (SOM) as required in the instant claims, especially in regard to claims 6-7, and 14-14).

Mangiameli et al. applied SOM and seven hierarchical methods to 252 messy data sets with real-world data imperfections such as dispersion, irrelevant variables, outliers, and nonuniform densities and found that self organizing map is significantly superior in both robustness and accuracy to other clustering methods. See pages 409-416.

The fact that Mangiameli et al. compare SOM and hierarchical clustering method for data analysis indicates that SOM and cluster analysis are art recognized equivalents for the same purpose, i.e. clustering analysis of data. Furthermore, since Mangiameli et al. demonstrates the superiority of SOM in its accuracy and robustness in data analysis, one of ordinary skill in the art would have been motivated to modify Mack to use SOM for the analysis of gene expression data.

Further, Mangiameli et al. teaches SOM clustering analysis of data from different sources. See pages 405-409. Thus, there would have been a reasonable expectation of success for modifying Mack and use SOM for the clustering analysis of gene expression data.

In regard to claim 2, the gene expression values are obtained from a gene that is subjected to at least one condition, such as chemical and irradiation treatment (columns 4 and 27).

In regard to claim 3, the step of receiving includes receiving gene expression values of datasets across multiple genes for a condition, such as detection of expression of multiple genes using oligonucleotide array (columns 13-28).

In regard to claim 4, Mack's methods comprising filtering out datapoints to identify genes whose expression is significantly altered (column 2).

In regard to claims 5, 9, 13, and 17, Mack's methods comprise normalizing the value of gene expression using a ratio of the signal for the test samples over the signal of the control probes (see column 17). It would have been well known to an ordinary skill in the art that standard deviation would be used in statistical analysis such as cluster analysis for normalization.

In regard to claims 8 and 16, it would have been obvious to an ordinary person in the art that the amount of outputting/displaying results would vary on the specific needs of individuals. One or more representatives from each cluster could be displayed.

In regard to claims 10 and 18, it would have been well known in the art that rescaling would often be necessary in a statistical analysis in order to accommodate the vast degree of difference in datasets.

In regard to claims 11 and 12, all the method steps and limitations have been set forth above.

Thus, the claimed invention would have been obvious to one of ordinary skill in the art at the time the invention was made in view of the combination of the teachings of Mack and Mangiameli et al. et al.

Applicant's arguments and the Declaration by Babriel Kreiman under 37 C.F.R. 1.132, both filed 7/14/03, have been fully considered but they are not persuasive.

The arguments of applicants and that in the Declaration by Kreiman essentially focus on the notion that Mack does not teach or suggest SOM, therefore, the combination of the cited references is improper. This is not deemed persuasive. As pointed out repeatedly in the previous Office actions, the motivation to combine the cited references is clear and obvious. The motivation is from Mangiameli et al., who thoroughly compare the pros and cons of SOM and seven clustering methods for analyzing data and concludes that SOM is superior to all others in determination of natural subgroups in a data set. Given the large number of genes used in Mack (65,000 for potential genes regulated by p53), one of ordinary skill in the art would have been motivated by Mangiameli to modify Mack by using SOM instead of cluster analysis. Thus the combination of the references is proper.

It appears that in the Declaration, Kreiman argues that the Mack reference teaches away of unsupervised method like SOM (pages 4-5). This is not found persuasive because, as set forth above, it is true that Mack does not explicitly teach or suggest SOM, however, it is also true that it does not teach away of the method. On the contrary, it suggests there are other methods out there that can be used. Clearly not teaching of something does not equate teaching away of it.

Further, both applicants and the Declaration by Kreiman assert that the instantly claimed invention has unexpected results (page 4 of applicants' argument and page 3 of the Declaration).

This is also not deemed persuasive because neither the applicant nor the Declaration actually provides any results that are unexpected.

### ***Conclusion***

No claim is allowed.

Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. §1.136 (a). A shortened statutory period for response to this final action is set to expire three months from the date of this action. In the event a first response is filed within two months of the mailing date of this final action and the advisory action is not mailed until after the end of the three-month shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136 (a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than six months from the mailing date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to:  
Shubo "Joe" Zhou, Ph.D., whose telephone number is (703) 605-1158. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

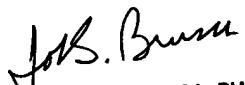
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

Art Unit: 1631

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst Tina Plunkett whose telephone number is 703)-305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

S. "Joe" Zhou, Ph.D.

Patent Examiner



JOHN S. BRUSCA, PH.D.  
PRIMARY EXAMINER